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09/720,530	03/12/2001	Preeti Lal	PF-0551 USN	2356

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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,530	LAL ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-41* is/are pending in the application.

4a) Of the above claim(s) *24-29 and 32-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,23,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on April 19, 2004 is acknowledged. The traversal is on the ground(s) that unity exists between all of applicant's claims and that the polypeptide sequences have corresponding features between them. This is not found persuasive because the claimed sequences are distinct physically, structurally, and functionally; and are therefore patentably distinct, each group from the other, and one sequence is not required to practice the other. The separate polypeptides and polynucleotides bear distinct structural or biochemical properties as substantiated by the separate SEQ ID numbers. Each group comprises separate and distinct nucleic or amino acid sequence or is a completely distinct product that does not share substantial structural features disclosed as being essential to the utility of the invention. Therefore, each disclosed patentably distinct polypeptide and polynucleotide is considered a separate invention.

Inventions drawn to the isolated polypeptides, polynucleotides and antibodies, as are related as different products. Both the products and methods are distinct because they have different structures, uses, functions, and effects and are capable of use one without the other. The methods of groups do not produce the same results and are therefore distinct as seen by each method group having different steps, functions and different final outcomes when compared to the other methods. Moreover, in view of the different steps, functions and different final outcomes each group is distinct and has a different special technical feature. Therefore, the products and methods of the

inventions are distinct as claimed and have separate special technical features. Moreover, the examination of all groups would require different searches in the U.S. Patent Shoes and the scientific literature and which would require the consideration of different patentability issues.

The requirement is still deemed proper and is therefore made FINAL.

2. Therefore, claims 24-29 and 32-41 have been withdrawn and claims 22-23 and 30-31, (SEQ ID NO:6) are under consideration in this office action.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 22-23 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 22-23 and 30-31 are drawn to an isolated polypeptide selected from the group consisting of: a) a polypeptide comprising an amino acid sequence of SEQ ID NO:6, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, c) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and d) an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6. Dependent claims are drawn to the polypeptide comprising SEQ ID NO:6, and a method of producing said polypeptide.

The written description in this case only sets forth the specific sequence, i.e., SEQ ID NO:6, therefore the written description is not commensurate in scope with the claims drawn to a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6. There is no guidance as to what the biologically-active and immunogenic fragments are; or what fragments can or cannot be used. The specification does not include structural examples of biologically-active and immunogenic fragments. The specification does not include structural examples of a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6. Thus, the

resulting polypeptides could result in a complexes not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). Applicant has failed to describe or show possession of a polypeptide comprising a naturally occurring amino acid sequence that is at least 90% identical to SEQ ID NO:6. It is noted that this naturally occurring polypeptide is being directed to nonstatutory subject matter and this naturally occurring polypeptide is not something which applicant invented or adequately described in the instant specification. There is no disclosure of biologically active fragments or immunogenic fragments from a polypeptide having SEQ ID NO:6. There is no teaching of a determination of which fragments are biologically active or immunogenic. Applicants' have failed to adequately describe such.

The claims drawn to polypeptides that fail to recite any associated function. Without an associated function there is no limit on the polypeptides encompassed by applicants' claims. It is noted that there is no requirement that the polypeptides have any activity. Furthermore any variant or derivative that has similar sequence identity yet has a different function is also encompassed by the claims. Thus, the functions of sequences have not been defined and thereby broaden the scope of the invention to encompass polypeptides not described by the instant specification. The specification

discloses SEQ ID NO:6, there is no disclosure of polypeptides sequences with 90% identity of SED ID NO:6. Thus, the structure of these polypeptides is not defined by the instant specification. Even though the claims recite a sequence identification number, the skilled artisan cannot envision the detailed structure of the encompassed naturally occurring polypeptides since the specification has not defined what the 10% variables can be.

With the exception of specifically named sequence, the skilled artisan did not envision the detailed structure of the a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of by only their structure does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Therefore only the recited sequences and not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

5. Claims 22-23 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

The claims are drawn to an isolated polypeptide selected from the group consisting of: a) a polypeptide comprising an amino acid sequence of SEQ ID NO:6, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, c) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and d) an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6. Dependent claims are drawn to the polypeptide comprising SEQ ID NO:6, and a method of producing said polypeptide.

However absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support, to one skilled in the art, as to whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. The claims encompass many possible variations and derivatives, including any substitution, insertion or deletion of any amino acids without any limitation. It is known for nucleic acids as well as proteins, for example that even a single nucleotide can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the recitation of similar sequence identity results in an unpredictable and therefore unreliable correspondence between

the claimed biomolecules and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement.

Several publications document the unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Russell [J. Mol. Bio.244:332-350]; Skolnick et al., [Trends in Biotech, 18(1):34-39]; and Attwood, [Science, 290:471-473, (29 October 2000)].

Applicants have not shown a representative polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, or a representative biologically active fragment or an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6. Applicants' have not disclosed the function or any physical characteristics of the claimed polypeptides and fragments. Applicants have not shown any representative examples. The specification fails to teach the identity of polypeptides comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, or a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, or an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6 as stated above in the Written Description Rejection, thus the claims are not enabled. The specification refers to unidentified polypeptides with unknown functions, thus the claims are not enabled.

In absence of further guidance from Applicants, the skilled artisan would have to de novo discover what the appropriate amino acid substitutions are and what critical

regions can and cannot tolerate such substitutions. Moreover, skilled artisans would have to de novo determine potential biologically active and immunogenic fragments. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. The need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for of the polypeptides. Therefore, a skilled artisan would be forced into undue experimentation to practice (i.e., make and use) the invention as is broadly claimed. Furthermore, one of skill in the art would not predict such a product would be structurally or functionally related to the instantly claimed polypeptide. Thus one of ordinary skill in the art could not make and/or use the invention as is broadly claimed. Such need for non-routine experimentation demonstrates that the specification is not enabled for to make and/or use the broadly claimed polypeptides. Accordingly, a skilled artisan would be forced into undue experimentation in order to make and/or use the invention as is broadly claimed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 22-23 and 30-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well-established utility.

Applicants have asserted several utilities for the claimed polypeptides referred to Neurotransmission Associated Protein (NTAP) such as in potential the treatment or prevention of neurological disorders, cancer, and immune disorders, therapeutics, and

diagnostic tools. However, these asserted utilities are neither specific nor substantial. The broadly claimed abilities is based on the claims drawn to an isolated polypeptide selected from the group consisting of: a) a polypeptide comprising an amino acid sequence of SEQ ID NO:6, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:6, c) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:6, and d) an immunogenic fragment of polypeptide having an amino acid sequence of SEQ ID NO:6.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (Trends in Biotech. 18:34-39, January 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Smith et al. (Nature Biotechnology 15:1222 and 1223, November 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (Trends in Genetics 15 (4):132-133, April 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, than

most homologs must have different molecular and cellular functions. Bork et al. (Trends in Genetics 12(10):425-427, October 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al. (Science 247:1306-1310, March 16, 1990) state that determination of three-dimensional structures from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted credible, specific and substantial utility of gene activity. The specification does not disclose a correlation between any specific function and the claimed polypeptides.

Accordingly, those skilled in the art cannot rely on this information to implement the processes of treatment or diagnosis. Given the lack of any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it not currently available in practical form the claimed isolated polypeptides is not credible, substantial or specific.

Claims 22-23 and 30-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if

Applicants were to evidence that claims 22-23 and 30-31 have a patentable utility they would be enable for the full scope of the invention.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 16, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600